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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,886	10/19/2004	Gihad Dargazanli	SSL0064	6340

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EXAMINER	
PERLINGER, SARAH E	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 01/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/511,886	DARGAZANLI ET AL.	
	Examiner	Art Unit	
	Sarah E. Perlinger	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-3, 5-16 are pending.

2. ***Oath/Declaration***

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application, by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration has reviewed and understands the contents of the specification, including the claims, as amended by any amendment specifically referred to in the oath or declaration.

It is suggested that applicant amend page 1 of the oath to read, "I/We have reviewed, understand the specification, claims and any amendments thereto of the above identified application".

Alterations to the Oath/Declaration must be initialed and/or dated (see 37 CFR 1.52(c)), or a newly signed Oath/Declaration must be submitted.

3. ***Specification***

The disclosure is objected to because of the following informalities: the title on page 1 of the specification is underlined by hand.

Appropriate correction is required.

The abstract of the disclosure is objected to because it is longer than one page. Correction is required. See MPEP § 608.01(b).

4. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 5, 8-9, 12-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The scope of claims 1-3, 5, 8-9, 12-14 cannot be ascertained due to the ambiguity of the phrase, a compound in the form of a "pure optical isomer". Pure to one person having ordinary skill in the art is not necessarily pure to another. It is unclear what the term "pure optical isomer" refers to. Therefore, the scope of claims 1-3, 5, 8-9, 12-14 cannot be ascertained.

Claims 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The scope of claim 12-16 cannot be ascertained due to the ambiguity of the phrase, a method for the treatment of disorders in which glycine transporters "are involved". The glycine transporters, Glyt1 and Glyt2 are confined to different areas of the nervous system and isoforms of the transporters have unique functions and characteristics (Caulfield et al., *J. Med. Chem.*, 2001, 44, 2679-2682). In addition, glycine transporters can both inhibit post-synaptic potentials and modulate excitatory neurotransmission (Lopez-Corcuera et al., *Molecular Membrane Biology*, 2001, 18 (1), 13-20). It is unclear what the term, "are involved" refers to. Therefore, the scope of claims 12-16 cannot be ascertained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The scope of the claims is drawn to a method of treating disorders in which glycine transporters are "involved" which broadly encompasses both post synaptic inhibitory and excitatory amino acid neurotransmission (see Lopez-Corcuera supra). No description was found for any compound to have contradictory inhibitory and excitatory activity in the specification.

Claims 12-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." The factors to be considered herein are those set forth as the In re Wands, 8 USPQ 2nd 1400 (1988) decision.

Nature of Invention

The claims are drawn to a method for the treatment of disorders in which glycine transporters are involved.

Scope of the Claims

The scope of the claims are drawn to a method for the treatment of disorders in which glycine transporters are "involved", which broadly encompasses both post synaptic inhibition and excitatory amino acid neurotransmission (see Lopez-Corcuera supra). No description was found for any compound to have contradictory inhibitory and excitatory activity in the specification.

The State of the art and Predictability

The state of the art in CNS intervention is highly unpredictable. The blood brain barrier protects the central nervous system from pathogenic organisms, toxic molecules, and even its own immune system. This barrier also prevents entry of possible therapeutic molecules into the brain. Presently, little is known about the molecular mechanisms which control the blood brain barrier (Daneman et al., *Cell*, 2005, 123, 9-12). Water-soluble materials which would ordinarily be taken up in the body, will not pass through the blood brain barrier causing drug delivery to the CNS to be an extremely difficult task (LeBowitz, *PNAS,* 2005, 102, 14485-14486).

The amount of guidance and working examples

The specification is limited to a description of *in vitro* and *ex vivo* activity. The Specification (pages 39-45) describes *in vitro* and *ex vivo* generic compounds' inhibition of the capture of glycine by glycine transporters. *In vitro* and *ex vivo* measurement in synaptic glycine re-uptake does not support such contradictory scope of the claims. In addition, *in vitro* and *ex vivo* measurements, although providing screening for leading compounds, does not provide description or enablement for CNS therapy for which factual evidence of passing the blood brain barrier, dosage, and site of administration, must be made known to one having ordinary skill in the art to practice such method. Section 112 requires the application itself to inform, not for others to fine out by themselves. Ex parte Aggarwal 23 USPQ 2nd 1481. In re Gardner 166 USPQ 138.

5. ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 5-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kikuchi et al. EP 0499995 in view of Froelich et al. (*J. Org. Chem.,* 1996, 61, 6700-6705) or Cheeseman et al. US 5,254,569.

Determination of the scope and content of the prior art (MPEP§ 2141.01)

Kikuchi et al. (EP 0499995) and Cheeseman et al. (US 5,254,569) disclosed generically the claimed anti-psychotic compounds and pharmaceutical compositions against the base claims as delineated. Explicit compounds are guided by the reference

(Cheeseman et al. US 5,254,569, Table 1, example 53) and render the claimed compounds generically encompassed.

Ascertainment of the difference between the prior art and the claims (MPEP § 2141.02)

The difference between the instant claims and the prior art compounds is that the instant claimed piperidinyl benzamide compounds are obtained in the form of pure optical isomers or in the form of a threo diastereoisomer. The reference however, disclosed generic teaching on the piperidinyl benzamide stereoisomers and their mixtures and racemates (Kikuchi et al. EP 0499995, page 4, lines 42-43) fully embracing the stereoisomers set forth in the instant claims. Furthermore, Froelich et al. taught in structurally analogous compounds, that the optical isomers can be separated and purified (see *J. Org. Chem.,* 1996, 61, page 6705).

Finding of prima facie obviousness-rationale and motivation (MPEP § 2142-2143)

One having ordinary skill in the art in possession of Kikuchi et al. EP 0499995 in view of Cheeseman et al. (US 5,254,569) and Froelich et al. (*J. Org. Chem.,* 1996, 61, 6700-6705) would be in possession of the instant claims **because** both prior art references are of analogous art. Kikuchi et al. discloses a compound with the same base structure as that of Freolich et al. (see EP0499995, formula (I) and *J. Org. Chem.,* 1996, 61, 6705). The compounds disclosed in both references also have the same utility in that they are used as active ingredients in pharmaceutical compositions (EP0499995, page 5 and *J. Org. Chem.,* 1996, 61, 6700). Specifically, Kikuchi et al. discloses the compounds as having utility in pharmaceutical compositions used for the treatment of psychotic disorders and neurotic diseases (EP0499995, page 5, lines 38-40). Furthermore, the generic disclosure by Kikuchi et al. fully encompassed the instant scope, and the specific teaching by Froeilich et al. to separate the optical isomers of structurally analogous compounds would render the threo diastereoisomer and optically pure form of the compounds obvious. One having ordinary skill in the art would be motivated to make such modification of separating the optical isomers, knowing that the biological system in stereospecific. "All biologically active molecules, hence all of life is 'left handed'. Your nerve receptors are optically active, so they respond differently to the different isomers, if they respond at all" (*Optical Isomers,* Newton BBS, 01/23/2006, Newton.dep.anl.gov).

6. Claims 1-3, 5, 8-9, 12-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 of copending Application No. 11/045247. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to the copending claims when A=N-R_1.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The instant claims 1-3, 5, 8-9, 12-14 have a narrower scope than the copending claims 1-7 of Application No. 11/045247. The difference between the instant claims and the copending claims, is that the benzamide of the instant claimed species has a trifluoromethyl substituent. Cheeseman et al. generically disclosed the base compound with the benzamide optionally substituted with one or more trifluoromethyl groups (US 5,254,569, column 2, lines 42-46). One having ordinary skill in the art in possession of the copending claims (Application No. 11/045247 claims: 1-7) and Cheeseman et al. would be in possession of the instant claims **because** both references are of analogous art. Cheeseman et al. (US 5,254,569, columns 2-3) disclosed a compound with the same base structure as that of claims 1-3 of copending Application No. 11/045247. The compounds disclosed in both references also have the same utility in that they are used as active ingredients in pharmaceutical compositions (see Cheeseman et al. claim 15 and claims 4-6 of Application No. 11/045247). One having ordinary skill in the art would be motivated to make such modification knowing that reasonable success has been demonstrated in analogous compounds. It is prima facie obvious to modify one known compound with *attributes* proven in analogous compounds.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a

nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. ***Conclusion***

None of the claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Sarah E. Perlinger, whose telephone number is (571) 272-5574. The examiner can normally be reached on Monday through Friday, 8:30 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Cecilia Tsang, can be reached at (571) 272-0562. The fax number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DP

01/18/2006

Celia Chang
Primary Examiner
Art Unit 1625